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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/974,519

10/10/2001

Dhiren R. Thakker

421/32/2

7285

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7590

04/10/2008

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EXAMINER

PACKARD, BENJAMIN J

ART UNIT

PAPER NUMBER

1612

MAIL DATE

DELIVERY MODE

04/10/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/974,519	Applicant(s) THAKKER ET AL.	
	Examiner Benjamin Packard	Art Unit 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-8 is/are pending in the application.
- 4a) Of the above claim(s) 4,5 and 7 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6 and 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1pg (02/25/2008)</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' arguments, filed 01/22/2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

Claims 1, 6, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cereijido et al., (Journal of Cell Science, 1993, Supplement 17, 127-132, see PTO-1449 dated 09/21/2007) in view of Grunicke et al., (Advan. Enzyme Regul., 1996, 36, 385-407, see PTO-1449 dated 09/21/2007).

Cereijido et al. (page 130: figure 4 and second column, first paragraph) teaches that inhibition of phospholipase C reduces the development of the transepithelial electrical resistance (TER, a measure for the paracellular transport through cells) and activation of phospholipase C increases TER. Thus, one of ordinary skill in the art would understand *a priori* that phospholipase C plays an important role in paracellular transport across the intestinal epithelium and that upon administration of a phospholipase C inhibitor the paracellular membrane permeability would be enhanced.

Grunicke et al. teaches that hexadecylphosphocholine (HePC, Miltefosine, n=15) is an inhibitor of PI-specific phospholipase C (page 393-395, see paragraph beginning

with 'The inhibition of PI-specific phospholipase C is a common denominator of all phospholipids analogues').

In regards to the formulation of the phospholipase C inhibitor for oral administration, as per Claim 8, it is cited in the instant specification that the formulation and dose preparation techniques are well known in the art. Examiner cites these references as evidence of Applicant's admission to the obviousness of administering orally the invention of the instant application (Oral administration being the route of administration elected by Applicant without traverse in the arguments/remarks submitted on 10 June 2003).

Applicants argue Cereijido et al is directed to the formation of tight junctions, not treating tight junctions already formed. Further, applicants argue that Grunicke et al does not teach HePC as an alkylphosphocholine.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., tight junctions are already formed) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claim 1 is directed to enhancing paracellular permeability at an absorption site (i.e. the membrane) by administering a phospholipase C inhibitor, at a time in which enhanced paracellular permeability is desired, thereby enhancing paracellular permeability. Therefore, where the time of enhancement can include when the cells are being created, the prior art indeed teaches increasing

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paracellular permeability. Additionally, membranes are constantly in flux, therefore the inhibition of additional tight junctions will indeed increase the paracellular permeability any time the phospholipase C inhibitor is administered. It should be further noted that the claim is directed to “enhancing paracellular permeability”, which interpreted broadly could include a minute increase. Therefore, the prevention of just one tight junction would be sufficient to read on the instant claims.

Finally, Grunicke et al was cited to show there are known alkylphosphocholines, such as HePC, which is an inhibitor of PI-specific phospholipase. Therefore, it would be obvious to one of skill in the art to use different inhibitors of the same PI-specific phospholipase when treating the same disease or condition.

Conclusion

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-F 8-3:45 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/
Patent Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612